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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/359,181	07/22/1999	GERARD GRASSY	1028-1	2476
110	7590	02/04/2004	EXAMINER	
DANN, DORFMAN, HERRELL & SKILLMAN 1601 MARKET STREET SUITE 2400 PHILADELPHIA, PA 19103-2307			CLOW, LORI A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 02/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/359,181

Applicant(s)

GRASSY ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,5,8-10,18-20 and 73 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,5,8-10,18-20 and 73 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed 24 November 2003, have been fully considered by they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1, 4, 5, 8-10, 18-20, and 73 are currently pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 1, 4, 5, 8-10, 18-20, and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims require a filtering step whereby candidate molecules are filtered using at least one dynamic filter. However, there is no description in the instant specification of said "dynamic filter". The specification describes a "static filter" at pages 33-35, which is well known in the art. However, there is no description of the "dynamic filter" that Applicant deems

as the novel, patentable invention. In the previous Office Action the Examiner assumed that the Multidyn software disclosed on page 17, line 21 was the dynamic filter. However, based upon the van de Waterbeemed Declaration, filed 24 November 2003, this seems not to be the case. Van de Waterbeemed, at point 11, letter e. states that the "Multidyn software is used to analyze trajectories and conformational spaces, i.e. it is merely an example of a convenient platform for applying PCA to autocorrelograms". The Examiner must then turn to the specification again for description of a dynamic filter, yet none is provided. Applicant states that a dynamic filter is described on pages 9 and 35-37. However, this does not provide a full and complete description as the specification merely describes components of a filter, such as Principal Component Analysis (PCA). One of skill in the art would not know what the particulars of the filter consist of by the description in the specification. It is generally considered that the terms "dynamic" and "filter" imply that change in response to some parameter is occurring and that selection for a desired outcome is made based upon or in response to the change. There is no description of these details in the specification.

Enablement

Claims 1, 4, 5, 8-10, 18-20, and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a

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determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to provide, identify, and describe molecules that exhibit a desired activity by determining molecular descriptors. This includes execution of a dynamic filtering step whereby candidate molecules are filtered using at least one dynamic filter representing constraints of conformational variations which each candidate molecule must satisfy in order to exhibit said desired activity. For the reasons discussed below, this constitutes undue experimentation.

b) and c) The specification provides examples for static filtering, as described on pages 33-35. Static filter screening is known in the art, as exemplified by Krieger et al. (Chemical and Engineering News (1996) Vol.74, pp.67-73) at page 68. The specification does not, however, describe the dynamic filtering process that the Applicant deems as the novel, patentable invention. Instead, the specification states at page 17, lines 19-24:

"Dynamic filtering can be carried out by means of new software designed by G. Grassy, the Multidyn software, which allows the conformational spaces at any molecules to be characterized on the basis of molecular dynamics trajectories. The bioactive conformations of the molecules in question are accordingly displayed."

However, as set forth in the van de Waterbeemd Declaration at point 11, letter e., the Multidyn software is not, per se, a dynamic filter.

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d) The invention is drawn to methods for dynamic filtering. However, the specification does not provide a means to do so without undue experimentation.

e) and g) It would have been well known in the art that static filtering could be performed and is described in several US Patents. One can refer to US 5,463,564 (Agrafiotis et al.) that describes a computer-implemented method to direct a combinatorial chemical library that includes a method to screen out compounds that are unsuitable. Further, US 5,025,388 (Cramer et al.) also teaches the CoMFA method which works by comparing the interaction energy descriptors of shape and relating changes in shape to differences in measured biological activity in a static way. Platt et al. (US 5,784,294) also teach a computer-based method (QSAR) for molecular descriptor that includes determining the shape of a molecule in a static way. All have been previously referenced and are evidence that static filtering was well known in the art of molecular descriptors.

The instant specification does not provide a description of a dynamic filter in an analogous way. The specification merely describes components of the filter, such as Principal Component Analysis (PCA) and Molecular Descriptor (MD) analysis (see pages 35-37). This is not a description of the dynamic filter itself. One of skill in the art would not know what the particulars of the filter consist of such that it could be used to select anything. Based upon a general understanding in the art for the terms “dynamic” and “filter,” a dynamic filter would consist of a means of changing in response to some parameter and selecting for or against something based upon or in response to the change. However, what, exactly, is changed (dynamic) and how to change it, is not described such that a one skilled in the art would know how to use such a filter.

h) The claims are fairly limited because they are drawn to filtering molecular descriptors by using a **dynamic** filter. The skilled practitioner would first turn to the instant specification for guidance to practice this method. However, the instant specification does not provide specific guidance to practice these embodiments. The instant specification merely mentions the use of a **new** software developed by one of the inventors of the instant application without describing how to use the software or the parameters that make the software function. In addition, as stated in the van de Waterbeemd Declaration, this is in fact not the dynamic filter, but simply a means to analyze trajectories and conformational space. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows only the use of static filtering and there is no guidance regarding dynamic filters. Finally, said practitioner would turn to trial and error experimentation to determine just what constitutes a “dynamic filter” and how to determine the parameters needed to implement a dynamic filter. Such represents undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 5, 8-10, 18-20, and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what the metes and bounds of “dynamic filter” encompass. As there is no description of such a filter in the specification, the meaning is vague and indefinite.

Declaration

The van de Waterbeemed Declaration submitted 24 November 2003 has been reviewed and considered. However, it is not persuasive for the reasons set forth above. Van de Waterbeemed sets forth, at point 10, that based upon consideration of the '181 application, the definition and general overview of the characteristics and use of dynamic filters at page 9, line 3 to page 10, line 22 are sufficient to enable any person skilled in the art to make or use a dynamic filter according to the invention. This is not persuasive in that at page 9, line 3 to page 10, line 22, components of the filter are described without describing the filter itself. The specification gives one example of a dynamic filter as one based on conformational space of the molecule and then states that distances between inactive and active molecules are calculated over time and then represented in an autocorrelogram. It is unclear from the description if the dynamic filter is responsible for selecting for certain atomic distances over time or all atomic distances over time. The role of the dynamic filter is not found in the instant specification. A static filter can perform the same function and it not described how the dynamic filter is any different from the static filter known in the art.

NO CLAIMS ARE ALLOWED.

Inquiries


Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (571) 272-0549.


MARJORIE MORAN
PATENT EXAMINER

January 30, 2004
Lori A. Clow, Ph.D.
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